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PPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,174	11/26/2003	Katrin Kneipp	M0925.70114US01	5755
759	90 08/11/2006		EXAMINER	
Timothy J. Oye			HINES, J	ANA A
Wolf, Greenfield 600 Atlantic Av			ART UNIT	PAPER NUMBER
Boston, MA 02210			1645	
			DATE MAILED: 08/11/2006	ς.

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action							
Before	the	Filing	of	an	Ap	peal	Brief

Application No.	Applicant(s)
10/723,174	KNEIPP ET AL.
Examiner	Art Unit
Ja-Na Hines	1645

Advisory Action	10/723,174	KINEIPP ET AL.	
Before the Filing of an Appeal Brief	Examiner	Art Unit	
	Ja-Na Hines	1645	
The MAILING DATE of this communication appe	ears on the cover sheet with the c	correspondence add	ress
THE REPLY FILED 17 July 2006 FAILS TO PLACE THIS APPI			
1. The reply was filed after a final rejection, but prior to or on this application, applicant must timely file one of the follow places the application in condition for allowance; (2) a No a Request for Continued Examination (RCE) in compliant time periods:	n the same day as filing a Notice of wing replies: (1) an amendment, affortice of Appeal (with appeal fee) in once with 37 CFR 1.114. The reply more	Appeal. To avoid abaidavit, or other evider compliance with 37 Cl	nce, which FR 41.31; or (3)
a) The period for reply expires 4 months from the mailing date b) The period for reply expires on: (1) the mailing date of this A no event, however, will the statutory period for reply expire! Examiner Note: If box 1 is checked, check either box (a) or TWO MONTHS OF THE FINAL REJECTION. See MPEP 7	Advisory Action, or (2) the date set forth ater than SIX MONTHS from the mailing (b). ONLY CHECK BOX (b) WHEN THE	g date of the final rejection	on.
Extensions of time may be obtained under 37 CFR 1.136(a). The date have been filed is the date for purposes of determining the period of exunder 37 CFR 1.17(a) is calculated from: (1) the expiration date of the set forth in (b) above, if checked. Any reply received by the Office later may reduce any earned patent term adjustment. See 37 CFR 1.704(b) NOTICE OF APPEAL	on which the petition under 37 CFR 1.1 tension and the corresponding amount shortened statutory period for reply orig r than three months after the mailing dal.	of the fee. The appropri inally set in the final Offi te of the final rejection, e	iate extension fee ce action; or (2) as even if timely filed,
 The Notice of Appeal was filed on A brief in comp filing the Notice of Appeal (37 CFR 41.37(a)), or any exte a Notice of Appeal has been filed, any reply must be filed AMENDMENTS 	nsion thereof (37 CFR 41.37(e)), to	avoid dismissal of th	is of the date of e appeal. Since
3. X The proposed amendment(s) filed after a final rejection,	but prior to the date of filing a brief	will not be entered by	ecanse
(a) ☑ They raise new issues that would require further co (b) ☐ They raise the issue of new matter (see NOTE belo (c) ☑ They are not deemed to place the application in being appeal; and/or	nsideration and/or search (see NO	TE below);	
(d) They present additional claims without canceling a NOTE: (See 37 CFR 1.116 and 41.33(a)).		ected claims.	
4. The amendments are not in compliance with 37 CFR 1.1		mpliant Amendment	(PTOL-324).
5. Applicant's reply has overcome the following rejection(s)		Aims also file al ama a malma	
 Newly proposed or amended claim(s) would be all non-allowable claim(s). 	nowable il submitted in a separate,	umely liled amendme	int canceling the
7. For purposes of appeal, the proposed amendment(s): a) how the new or amended claims would be rejected is pro The status of the claim(s) is (or will be) as follows: Claim(s) allowed: None.		ll be entered and an e	explanation of
Claim(s) objected to: <u>None</u> .			
Claim(s) rejected: <u>188-195 and 198-201</u> . Claim(s) withdrawn from consideration: <u>1-17,19,23-37,39</u> AFFIDAVIT OR OTHER EVIDENCE	<u>,43-58,60,64-72,74,78-85,87,91-11</u>	7,122,125,126 and 1	<u>28</u> .
B. The affidavit or other evidence filed after a final action, bu because applicant failed to provide a showing of good an was not earlier presented. See 37 CFR 1.116(e).			
9. The affidavit or other evidence filed after the date of filing entered because the affidavit or other evidence failed to of showing a good and sufficient reasons why it is necessar	overcome <u>all</u> rejections under appe y and was not earlier presented. S	al and/or appellant fai ee 37 CFR 41.33(d)(ils to provide a 1).
10. ☐ The affidavit or other evidence is entered. An explanatio REQUEST FOR RECONSIDERATION/OTHER	n of the status of the claims after e	ntry is below or attach	ied.
11. The request for reconsideration has been considered but	ut does NOT place the application in	n condition for allowar	nce because:
12. Note the attached Information Disclosure Statement(s). 13. Other:	(PTO/SB/08 or PTO-1449) Paper N		
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Claims 130, 132-135,138,139,146,147,153,155-157,159-162,164,172,179,180,182,183, 187 and 196-197 have been withdrawn.

The after final amendment raises new issues that would require further search and/or consideration. The new issues are drawn to the method for determining a sequence wherein sequentiall identifying y raman spectroscopy involves analyzing raman data in which at leasr one spectral line represent a single nucleotide. Furthermore, the amendment presents new claim 202 without cancelling any of the finally rejected claims. Thus, the amendment will not be entered.

The rejection of claims 188-195 and 198-201 under 35 U.S.C. 102(b) as being anticipated by Vo-Dinh (US Patent 5,306,403) is maintained for reasons already of record. Applicants argue that Vo-Dinh uses known sequences while the instant method uses unknown sequences. However a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Furthermore, the claims do not limit the uses of known or unknown sequences, therefore the argument is not persaussive.

Applicants assert that Vo-Dinh uses fragments of 4 to 8 bases. However the instant claims recite fragmenting one or more bases, therefore the instant claims embrace fragments of 4 to 8 bases and there is no limitation on the size of the fragments. Therefore the art reads on the instant claims.

Applicants assert that it is unclear how raman spectroscopy is used by Vo-Dinh et al. However Vo-Dinh et al., clearly teach how the label is a specific chemical group tand can be detected using SERS spectrographic techniques. Vo-Dinh et al., teach that after separation of the DNA fragments, the SERS labels are detected by focusing a light source onto a surface of a SERS-active coating. Then a sequencer apparatus allows for sequential identification. The claims only require that the fragments are sequentially identified by raman spectroscopy and that the determination of the sequence is based on the identification. There is no requirement that only Raman Spectroscopy techniques be used. Furthermore, Vo-Dinh et al., teach raman-based SER(R)S analysis systems for DNA sequencing. Therefore, Vo-Dinh et al., clearly teach DNA sequence analysis, thus the rejection is maintained.

The rejection of claims 188-195, 198-199 and 201 under 35 U.S.C. 103(a) as being unpatentable over Dorre et al., in view of Kneipp et al., is maintained for reasons already of record. Applicants argue that there is no suggestion to combine the references. In response to applicant's argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, it would have been prima facie obvious at the time of applicants invention to modify the method for determining a sequence of at least a portion of a DNA or an RNA as taught by Dorre et al., wherein the modification exchanges fluorescence detection for SERS detection as taught by Kneipp et al., because Kneipp et al., teaches that raman spectroscopy is complementary to fluorescence but offers additional beneficial properties.

Applicants' urge that hindsight reasoning was used to make the rejection. However, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In this case one of ordinary skill in the art would have a reasonable expectation of success in determining the sequencing method using raman spectroscopy instead of fluorescence since it provides a high degree of structural information about the molecule; requires shorter time for detection and avoids photodecomposition. Furthermore, no more than routine skill would have been required to exchange the detection methods when both methods are known to detect single molecules, and the art teaches that single molecule detection can identify DNA or RNA sequences using nuclease fragmentation and sequential identification and determination of the sequence. Therefore applicants' arguments are not persaussive and the rejection is maintained.